

1 parallel plate flow chamber. The WSS in these devices
2 is usually steady because of difficulties in simulating
3 pulsatile flow. Cyclic straining devices provide only
4 strain, by stretching cells on a compliant membrane
5 without flow. Both types of systems are thus limited by
6 their design. However, no studies have been performed
7 studying both parameters (WSS and CS) using cells grown
8 on a single type of support surface because such a
9 system, until now, has remained technologically
10 unfeasible. The present invention addresses and solves
11 this long-felt need by providing a system in which
12 endothelial cells can be grown on a single support
13 surface, and subjected to studies in which both wall
14 shear stress and circumferential strain can be examined
15 independently of each other.--

16
17 Please replace the paragraph beginning at page 10, line 18, with the
18 following rewritten paragraph:

19
20 --The present invention is a system for
21 hemodynamic simulation comprising a vessel having
22 properties of a blood vessel, a reservoir containing a
23 quantity of fluid, tubing connecting the vessel and
24 reservoir, and at least one pump for circulating the
25 fluid within the system. Fluid can be tissue culture
26 medium or blood analog fluid, and the vessel may include
27 mammalian cells attached to its inside. A drive system,
28 comprising two reciprocating drive shafts that are
29 coupled by a cam, enables the uncoupling of pulsatile
30 flow and pulsatile pressure to provide independent
31 control over wall shear stress and circumferential
32 strain. The shaft drives two pumps that are 180 degrees
33 out-of-phase and are connected upstream and downstream
34 of the vessel, and effect this uncoupling.--

35
36 Please replace the paragraph beginning at page 15, line 18, with the

1 following rewritten paragraph:

2
3 --Each of pumps 40 and 42 is under the control of
4 a drive system unit 44, which comprises a plurality of
5 independent linear actuators 46. These actuators 46 can
6 be individual, stand alone units, for may be controlled
7 by one or more computer systems 48. In the embodiment
8 in Fig. 1A, the second pumps 40 are connected by a shaft
9 50, and the third pumps 42 are connected by a second
10 shaft 52. In one embodiment of the present invention,
11 in which a 4-bar linkage mechanism is the drive system,
12 a cam 54 affects the control of the various second pumps
13 40 and third pumps 42. In one embodiment of the present
14 invention (Fig. 1B) the drive system unit 44 comprises
15 six computer-controlled linear actuators, while in
16 another embodiment (Fig. 1A) the drive system unit 44
17 comprises four independent computer-controlled linear
18 actuators.--

19
20 Please replace the paragraph beginning at page 14, line 1, with the
21 following rewritten paragraph:

22
23 --A pressure sensor 18 is used for monitoring the
24 internal system pressure, and positioned either upstream
25 and/or downstream of the compliant vessel 12. A
26 pressure sensor can also be placed in the external
27 chamber 36 to monitor external chamber pressure.
28 Pressure sensor 18 can also be a blood pressure catheter
29 (such as, for example, and not intended as a limitation,
30 a MILLAR® catheter (MPC-500 with pressure meter TCB500;
31 Registered Trademark of Millar Instruments Corp.,
32 Houston TX), in either a fluid contacting or non-
33 contacting version. Pressure sensor 18 may also be a
34 pressure probe, such as those known to those skilled in
35 the art. In one embodiment of the present invention,
36 the pressure sensor is a catheter tip transducer

1 (Millar) which is inserted upstream into the lumen of
2 the compliant vessel. Where cells are being used in the
3 compliant vessel 12, the pressure sensor 18 is kept
4 upstream to avoid damaging the cells. Pressure drop
5 across the compliant vessel has been shown to be
6 negligible.--

7
8 Please replace the paragraph beginning at page 23, line 28, with the
9 following rewritten paragraph:

10
11 --In this example, the vessel chosen for growth of
12 endothelial cells is a silicone tubing, sold by Dow-
13 Corning, Midland, MI under the brand name of SYLGARD
14 184® elastomer, or Silastic (MDX4-4210), Medical Grade
15 tubing, and used to prepare elastic artery models.
16 These models were prepared using the method described by
17 Lee and Tarbell (1997, and hereby incorporated by
18 reference), and included the preparation of models of
19 human linear and bifurcating arteries.--

20
21 Please replace the paragraph beginning at page 25, line 17, with the
22 following rewritten paragraph:

23
24 --Requirements of the fluid 16 include having a
25 viscosity that can be elevated to achieve conditions of
26 physiologic stress at modest flow rates. Dextran is
27 used within the fluid while the present invention uses
28 vessels of approximately 0.79 cm diameter; in instances
29 employing vessels of smaller diameter, addition of
30 dextran is not necessary. The fluid should be free of
31 Phenol Red and serum so as not to interfere with
32 measurements of other cellular products, such as
33 prostacycline or nitric oxide. Serum and other
34 substances can be added to the media if these substances
35 are under study, or if the serum or substance is
36 required by the cell line.--

1 Please replace the paragraph beginning at page 27, line 35, with the
2 following rewritten paragraph:
3

4 --Example 1 described the use of vessel models,
5 modeled after the structure and material properties of
6 actual human aortic vessels. In addition to using
7 models of vessels, other vessels can be used in
8 conjunction with the present invention. These can be
9 chosen from the group consisting of an artery, an
10 artificial artery, a vein, human umbilical tissue, or a
11 non-rigid tube. The artery may comprise a bovine aorta,
12 or a human coronary artery. The vein may comprise
13 bovine veins, or human veins such as a human leg vein or
14 a human umbilical vein. Bovine tissue can be obtained
15 from commercial supply sources, such as Vec
16 Technologies, Ithaca NY and human umbilical materials
17 can be obtained a local hospital, or a commercial
18 sources such as Clonetics, Vec Technologies, or other
19 sources known to those skilled in the art. In addition
20 to studying the effects of hemodynamic conditions on
21 endothelial cells, other types of cells can also be
22 used, including smooth muscle cells, cartilage cells,
23 osteocytes, embryonic and adult stem cells, and the
24 like.--
25

26 In the Claims:
27

28 Please amend Claims 2-4, inclusive, and Claim 6.
29

30 Please add Claims 7-53, inclusive.
31

32 2. (Amended) The system as described in claim 11, wherein the vessel
33 preferably is a model of a mammalian blood vessel.
34

35 3. (Amended) The system as described in claim 11, wherein the vessel
36 is biocompatible.